PHOX2B gene

paired like homeobox 2b

Normal Function

The *PHOX2B* gene provides instructions for making a protein that acts early in development to help promote the formation of nerve cells (neurons) and regulate the process by which the neurons mature to carry out specific functions (differentiation). The protein is active in the neural crest, which is a group of cells in the early embryo that give rise to many tissues and organs. Neural crest cells migrate to form parts of the autonomic nervous system, which controls body functions such as breathing, blood pressure, heart rate, and digestion. Neural crest cells also give rise to many tissues in the face and skull, and other tissue and cell types.

The protein produced from the *PHOX2B* gene contains two areas where a protein building block (amino acid) called alanine is repeated multiple times. These stretches of alanines are known as polyalanine tracts or poly(A) tracts.

Health Conditions Related to Genetic Changes

congenital central hypoventilation syndrome

Most *PHOX2B* gene mutations that cause congenital central hypoventilation syndrome (CCHS) add extra alanines to the polyalanine tracts in the PHOX2B protein. This type of mutation is called a polyalanine repeat expansion. Other types of *PHOX2B* gene mutations have been identified in 8 to 10 percent of individuals with this disorder.

Mutations are believed to interfere with the PHOX2B protein's role in promoting neuron formation and differentiation, especially in the autonomic nervous system, resulting in the problems regulating breathing and other autonomic nervous system dysfunction seen in CCHS.

neuroblastoma

Several mutations in the *PHOX2B* gene have been identified in people with neuroblastoma, a type of cancerous tumor composed of immature nerve cells (neuroblasts). Neuroblastoma and other cancers occur when a buildup of genetic mutations in critical genes—those that control cell proliferation or differentiation—allow cells to grow and divide uncontrollably to form a tumor. In most cases, these genetic changes are acquired during a person's lifetime, called somatic mutations. Somatic mutations are present only in certain cells and are not inherited. Less commonly, gene mutations that increase the risk of developing cancer

can be inherited from a parent. Both types of mutation occur in neuroblastoma. Somatic mutations in the *PHOX2B* gene increase the risk of developing sporadic neuroblastoma, and inherited mutations in the *PHOX2B* gene increase the risk of developing familial neuroblastoma.

In some people with neuroblastoma, mutations in the *PHOX2B* gene change a single protein building block (amino acid) in the PHOX2B protein. Other affected individuals may have an addition or deletion of several DNA building blocks (nucleotides) in the *PHOX2B* gene. Addition or deletion of nucleotides changes the sequence of amino acids in the PHOX2B protein. All of these types of mutations have been found in familial and sporadic neuroblastoma. The mutations are believed to interfere with the PHOX2B protein's role in promoting nerve cell differentiation, which results in an excess of immature nerve cells and leads to neuroblastoma.

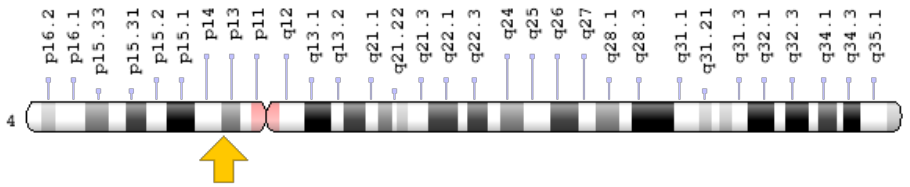
other disorders

Variations in the *PHOX2B* gene have been associated with increased risk of certain other disorders involving the autonomic nervous system and tissues derived from the neural crest. Particular *PHOX2B* gene variations have been identified in people who have both congenital central hypoventilation syndrome and a dysfunction of the nerves in the intestine called Hirschsprung disease (this combination of disorders is often called Haddad syndrome). The nerve problems in Hirschsprung disease result in severe constipation, intestinal blockage, and enlargement of the colon in affected individuals. *PHOX2B* gene mutations have also been identified in people with both neuroblastoma and Hirschsprung disease. In addition, *PHOX2B* gene variations have been identified in some babies who died of sudden infant death syndrome (SIDS). *PHOX2B* gene variations likely affect the regulation of neuron differentiation in early development, resulting in an increased risk of these disorders.

Chromosomal Location

Cytogenetic Location: 4p13, which is the short (p) arm of chromosome 4 at position 13

Molecular Location: base pairs 41,744,082 to 41,748,970 on chromosome 4 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- NBLST2
- NBPhox
- neuroblastoma paired-type homeobox protein
- neuroblastoma Phox
- paired-like homeobox 2b
- paired mesoderm homeobox 2b
- Phox2b
- PHOX2B homeodomain protein
- PHX2B_HUMAN
- PMX2B

Additional Information & Resources

GeneReviews

- Congenital Central Hypoventilation Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1427

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28PHOX2B%5BTIAB%5D%29+OR+%28paired-like+homeobox+2b%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- HIRSCHSPRUNG DISEASE, SUSCEPTIBILITY TO, 1
  http://omim.org/entry/142623
- PAIRED-LIKE HOMEOBOX 2B
  http://omim.org/entry/603851

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/PHOX2BID126ch4p13.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PHOX2B%5Bgene%5D

- HGNC Gene Family: PRD class homeoboxes and pseudogenes
  http://www.genenames.org/cgi-bin/genefamilies/set/521
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=9143
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/8929
- UniProt
  http://www.uniprot.org/uniprot/Q99453

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